What is claimed is:

1) A method for improving the binding affinity of a ligand for a biological target comprising:
   a) preparing first NMR spectra of a first complex comprising the biological target and a paramagnetically labeled derivative of a first ligand;
   b) preparing second NMR spectra of a second complex comprising the biological target and a second ligand; and
   c) analyzing the spectra to determine whether the second ligand binds to the biological target within the paramagnetic zone of the paramagnetically labeled derivative;

wherein steps (a) and (b) are performed simultaneously, consecutively, or in any order.

2) The method of claim 1 wherein step (c) is performed by:
   a) identifying peaks on the first NMR spectra that are perturbed by the paramagnetic label; and
   b) determining whether the second ligand perturbs peaks on the second NMR spectra that are also perturbed by the paramagnetic label.

3) The method of claim 1 wherein the first complex further comprises the second ligand, and step (c) is performed by determining whether the paramagnetically labeled derivative of the first ligand perturbs peaks associated with the second ligand.

4) The method of claim 3 further comprising, before step (c), preparing third NMR spectra of a mixture of the paramagnetically labeled derivative of the first ligand and the second ligand in the absence of the biological target.

5) The method of claim 1 further comprising:
   a) deducing the relative three-dimensional orientation and distance of separation of the first and second ligands when bound to the biological target; and
   b) selecting or preparing a compound that contains the first and second ligands substantially in the relative orientation and distance.

6) The method of claim 5 wherein the distance of separation is determined as a function of the loss of intensity for NMR resonances from the second ligand.

7) The method of claim 5 wherein the three dimensional orientation is deduced by producing a field ordered state in a medium comprising the biological target, the first ligand, and the second ligand, and analyzing dipolar couplings within the first and second ligands.

8) The method of claim 7 wherein the field ordered state is produced by an aqueous dispersion of lipid bicelles having complementary charges to the biological target.

9) The method of claim 7 wherein the field ordered state is produced by an aqueous dispersion of bacteriophage having a domain of the biological target in the outer coat.

10) The method of claim 1 wherein the paramagnetic label is a nitroxide or metal chelate.

11) The method of claim 1 wherein the first and second NMR spectra are two dimensional HSQC spectra.

12) The method of claim 1 wherein the biological target is isotopically labeled.

13) The method of claim 1 wherein the biological target is a protein, and NMR resonances from the protein are not assigned to a sequence of the protein.

14) The method of claim 5 wherein the biological target is a protein, and the three dimensional conformation of the protein is unknown.

15) The method of claim 1 wherein the first ligand is an oligosaccharide, and the biological target is a protein.

16) The method of claim 1 wherein the second complex comprises the first ligand, or a paramagnetically labeled derivative thereof.

17) A method for improving the binding affinity of ligands for biological targets comprising:

a) preparing first NMR spectra for a first complex comprising the biological target and a paramagnetically labeled derivative of a first ligand;

b) identifying peaks on the first NMR spectra that are perturbed by the paramagnetic label;

c) preparing second NMR spectra for a second complex comprising the biological target and the second ligand, and

d) determining whether the second ligand perturbs peaks on the second NMR spectra that are also perturbed by the paramagnetic label;

wherein said steps are performed sequentially, simultaneously, or in any order.

18) The method of claim 17 further comprising:

a) deducing from the NMR spectra the distance between the first and second ligands when bound to the biological target;

b) deducing from the NMR spectra the relative three dimensional orientation of the first and second ligands when bound to the biological target; and

c) selecting or preparing a hybrid ligand that contains the first and second ligands covalently linked substantially at the bond distance and relative orientation deduced in steps (a) and (b).

19) A method for improving the binding affinity of ligands for biological targets comprising:

a) preparing first NMR spectra of a first complex comprising a biological target, a paramagnetically labeled derivative of a first ligand, and a second ligand;

b) preparing second NMR spectra of a second complex comprising the biological target and either the second ligand or the paramagnetically labeled derivative of the first ligand;

c) preparing third NMR spectra of a mixture of the paramagnetically labeled derivative of the first ligand and the second ligand in the absence of the biological target; and

d) analyzing the spectra to determine whether the paramagnetically labeled derivative of the first ligand perturbs peaks associated with the second ligand;

wherein steps (a), (b), and (c) can be performed simultaneously, consecutively, or in any order.

20) The method of claim 19 further comprising:

a) deducing from the NMR spectra the distance between the first and second ligands when bound to the biological target;

b) deducing from the NMR spectra the relative tree dimensional orientation of the first and second ligand when bound to the biological target; and

c) selecting or preparing a hybrid ligand that contains the first and second ligands covalently linked substantially at the bond distance and relative orientation deduced in steps (a) and (b).

21) A method of increasing the binding affinity of two or more ligands for a protein comprising:

a) deducing from NMR spectra the distance between first and second ligands when bound to a protein,

b) deducing from NMR spectra the relative three-dimensional orientations of the first and second ligands when bound to the protein, and

c) selecting or preparing a compound that contains the first and second ligands substantially in the relative three-dimensional orientations determined in step (b) substantially at the distance determined in step (a),

d) wherein:

i) NMR resonances assigned to a sequence of the protein are not used for step (a),

ii) the three dimensional configuration of the protein is not used for step (b),

iii) the first and/or second ligand is a mono-, oligo-, or polysaccharide,

iv) the first and/or second ligand is not in rapid exchange when bound to the protein, or

v) NMR observable protons on the first and second ligands are not sufficiently close to the surface of the protein to characterize the relative three-dimensional orientation of the ligands by NOEs.

22) The method of claim 21 wherein NMR resonances assigned to a sequence of the protein are not used for step (a).

23) The method of claim 21 wherein the three dimensional configuration of the protein is not used for step (b).

24) The method of claim 21 wherein the first and/or second ligand is a mono-, oligo-, or polysaccharide.

25) The method of claim 21 wherein NMR observable protons on the first and second ligands are not sufficiently close to the surface of the protein to characterize the relative three-dimensional orientation of the ligands by NOEs.